SUMMARY OF INTERVIEW

Attendees, Date and Type of Interview

The interview was conducted on June 24, 2008 and attended by Thomas Arno and Exmainers Susan Fernandez and Blaine Lankford.

Exhibits and/or Demonstrations

None

Identification of Claims Discussed

Claims 1-7.

Identification of Prior Art Discussed

Catterall and Connelly

Proposed Amendments

None

Principal Arguments and Other Matters

Applicant argued that the combination of Catterall and Connolly does not teach or suggest using external electrodes to produce gradual changes in transmembrane potential over the ocurse of a series of electric field pulses.

Results of Interview

Applicant agreed to submit a supplemental amendment clarifying the nature of the transmembrane potential change and the detection of effects of drug candidates on the ion channels.

REMARKS

Amendments to the Claims

Claims 1-7 are pending in the application. Claim 1 has been amended. Support for amendments to Claim 1 related to setting the transmembrane potential can be found, for example, in paragraphs [0207] and [0377] of the specification as published in Publication No. 2004/0191757. Support for the amendment related to detection can be found in paragraphs [0270] and [0431] of this publication. No new matter has been added.

Claim Rejection under 35 U.S.C. § 112, ¶2

Claim 1 has been amended in accordance with the Examiner's suggestion to remove the term "substantially" from the claim. Applicant thus respectfully requests the Examiner's rejection be withdrawn.

Rejection of Claims under 35 U.S.C. § 103(a)

Claims 1, 2 and 4-6 are rejected under 35 U.S.C. §103(a) as obvious in light of U.S. Pat. No. 5,437,982 to Catterall et al. ("Catterall") in view of Connolly et al., Biosensors and Bioelectronics, 1990 5: 223-234 ("Connolly").

Independent Claim 1 has been amended to recite, inter alia, modulating a transmembrane potential of cells with a series of electric field pulses "so as to set said transmembrane potential to a level corresponding to a pre-selected voltage dependent state of [a] target ion channel, wherein the frequency of the electric field pulses (f) is within the range $\tau_M^{-1} \leq f \leq \tau_b^{-1}$ where τ_M is a time constant for decay of transmembrane potential changes, and τ_b is an average target ion channel open time wherein the pulses at said frequency cause a sustained transmembrane potential change via a stepwise accumulation or loss of ions over the course of said series of pulses."

Catterall does not teach applying pulses at a rate that causes a sustained change in transmembrane potential via a stepwise accumulation or loss of ions over the course of the series of pulses as recited in Claim 1. Because Catterall uses a patch clamp, the transmembrane

potential will follow the pulse amplitude up and down with each applied pulse regardless of their rate. The potential will not change over the course of the series of electric fields pulses.

Similarly, Connolly does not teach using a pulse frequency to cause a sustained change in transmembrane potential via a stepwise accumulation or loss of ions over the course of the series of pulses. Connolly discloses stimulation of cardiac myocyte cells using a "slow (1 Hz) biphasic square wave applied to the stimulating electrode. . . . If beating commenced [in the cardiac cells] then the removal of the stimulus did not cause its cessation." See Connolly at page 232. Causing myocytes to beat with application of one or more electrical pulses is not a sustained change in transmembrane potential produced with stepwise ion accumulation or loss in the cell over the course of a series of electric field pulses.

The applicant wishes to emphasize that stimulation with extracellular electrodes has dramatically different effects from patch clamping. The Examiner's assertion that Connolly points out that extracellular electrodes are a suitable substitute for an intracellular patch clamp is not accurate. Just because extracellular electrodes can initiate beating does not mean they are "suitable substitutes" for a patch clamp. The Examiner is referred to Figures 10 and 14 of the application which illustrate examples of the sustained changes made possible with the claimed method. This is qualitatively different form the beating produced by Connolly. Prior to the present invention, no one thought that external electrodes could be used to set transmembrane potential to a desired level, and Connolly is consistent with this conventional outlook on the effects of extracellular electrodes.

As described in paragraph [0375] of the specification as published, embodiments of the invention of Claim 1 do not require pharmacological agents or patch clamping to modulate transmembrane potential. Pharmacological agents have limited and specific effects which accordingly limits their range of usefulness. Patch clamping is slow and labor intensive, and can result in loss of cellular content. With the invention of Claim 1, a wide variety of screening procedures can be performed in a flexible, low cost manner.

The remaining prior art of record does not cure either of the above-mentioned deficiencies. Thus, Applicants respectfully request the Examiner's rejection of independent amended Claim 1 be reconsidered and withdrawn. Claims 2-7 are dependent on amended Claim

1. It is respectfully submitted that these claims are patentable for at least the same reasons as set forth above with regard to amended independent Claim 1.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

The Applicants have endeavored to address all of the Examiner's concerns as expressed in the previous Office Action. Accordingly, arguments in support of the patentability of the pending claim set are presented above. In light of these amendments and remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested. If any issues remain that could be resolved by telephone, the Examiner is invited to call the undersigned directly.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 7/23/08

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